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(54) Title: **CONTROLLED-DISSOLVING POLYMERIC DEVICE FOR THE ORAL CAVITY**

(57) Abstract: The invention is directed to a solid, controlled-dissolution composition for the oral cavity that adheres to hard dental surfaces, such as natural teeth and the surrounding soft tissue, and which creates a physical barrier to painful stimuli associated with dentinal hypersensitivity.

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**CONTROLLED-DISSOLVING POLYMERIC DEVICE FOR THE ORAL
CAVITY**

5 FIELD OF THE INVENTION.

This invention relates to compositions for the treatment of dentinal hypersensitivity and methods for treating dentinal hypersensitivity. In particular, this invention relates to a sustained- or controlled-dissolution composition for the oral cavity that adheres to the natural teeth and/or gums, and which comprises agents
10 capable of creating a physical barrier to dentinal hypersensitivity and/or which comprises pharmaceutical agents for the treatment of dentinal hypersensitivity.

BACKGROUND OF INVENTION

Dentinal hypersensitivity is a temporary induced pain sensation produced
15 when hypersensitive teeth are subjected to changes in temperature and/or pressure or to chemical action. Hypersensitivity may occur whenever attrition or abrasion exposes the dentin of a tooth, or when the tooth's finer root surface is exposed by periodontal disease. Dentin is a bone-like material in teeth that is usually covered by enamel above the gum line and cementum below the gum line. The enamel or
20 cementum may be removed through decay, injury, disease or other causes, thereby exposing the dentin to external stimuli in the mouth. Dentin generally contains channels, called tubules, that allow material and energy transport between the exterior of the dentin and the interior of the tooth where the nerve is located.

One theory of dentinal hypersensitivity, called the hydrodynamic theory,
25 suggests that exposure of these tubules to external stimuli can cause irritation of the nerve and lead to the discomfort of hypersensitivity. The hydrodynamic theory suggests that hypersensitivity may be treated by making the nerve in the tooth less sensitive to stimuli (called nerve desensitization), or by blocking or occluding the tubules to prevent or limit exposure of the nerve to external stimuli.

30 Many attempts have been made to control dentinal hypersensitivity. One approach is to reduce the excitability of the nerve in a sensitive tooth. This technique interferes with the ordinary triggering process of the nerve by altering the chemical environment of the nerve through the use of agents to make the nerve less sensitive. These agents are generally referred to as "nerve agents" or "nerve
35 desensitizing agents". By making the nerve less sensitive, the effect on the nerve of any external factors that are able to penetrate the tubules, is reduced. Any nerve desensitizing agent that is a neuroactive substance, i.e., any ion or salt that has a pain

reducing or analgesic activity, is suitable for use in the composition of the present invention.

The most well-known agent for this purpose is potassium nitrate, used in commercial dentifrices for sensitive teeth and discussed in U.S. Patent No.

5 3,863,006. Examples of other agents known as nerve desensitizing agents are found in the following U.S. patents: potassium salts such as potassium bicarbonate and potassium chloride, U.S. Patent Nos. 4,631,185 and 4,751,072; strontium and fluoride ions, U.S. Patent No. 4,990,327; and zinc and strontium ions, U.S. Patent No. 3,888,976.

10 Another approach to control dentinal hypersensitivity, as discussed above with regard to the hydrodynamic theory, is the use of agents to fully or partially occlude tubules. Tubule occluders serve to seal or block the dentin tubules thereby diminishing the effect of external stimuli such as changes in temperature, pressure, ionic gradients or contact with chemical irritants, as well as helping to reduce the
15 flushing of potassium from the tubules by natural outward flow of dentinal fluid. Examples of materials which are used as tubule blocking agents include materials having a particle size smaller than that of a dentin tubule for blocking the dentin tubules; and materials that can produce an agglomerate within the dentin tubules and/or form a precipitate that will deposit onto the dentinal surface. Specific
20 examples of such "tubule blocking agents" are found in the following patents: charged polystyrene beads, U.S. Patent No. 5,211,939; apatite, U.S. Patent Nos. 4,634,589 and 4,710,372; a polyacrylic acid polymer having a typical molecular weight from about 450,000 to about 4,000,000, U.S. Patent No. 5,270,031; and water-soluble or water-swellaable polyelectrolytes or salts thereof, U.S. Patent No.
25 4,362,713. In addition, U.S. Patent No. 5,589,159 discloses the use of Laponite or hectorite clay to seal dentinal tubules.

PCT Patent Application WO 00/042981 discloses a different mode of action wherein a composition of two different desensitizing agents (stannous fluoride and potassium nitrate) is separated in a dual phase dispensing unit. These agents are
30 separated in the disclosed compositions to enhance their stability. Further, WO 02/15809 discloses a synergistic combination of at least one tubule occluding agent and one nerve-desensitizing agent.

While these approaches have achieved a certain level of success, there is a need for a portable and inconspicuous treatment for tooth sensitivity and the pain
35 associated therewith, that is local in application providing fast acting relief over a discreet, but extended time period. The oral care device of this invention achieves these goals by providing a sustained- or controlled-dissolution composition for the

oral cavity that creates a barrier to painful stimuli associated with dentinal hypersensitivity.

The most significant problem in delivering any active to the dentin or nerve is the outward flow of dentinal fluid. Therefore, by creating a barrier over dentinal
5 tubules, the dentinal fluid flow is reduced or eliminated. In addition to simply creating a barrier to pain, the reduction/elimination of fluid flow provides an enhanced environment for penetration of an active to the nerve.

Oral controlled-release delivery systems are well known in the pharmaceutical field and include the ability to maintain a desired level of
10 medicament over a desired period of time. The art describes free forms, such as sublingual tablets, troches and buccals. In addition to non-attached oral sustained- or release forms, other forms are designed to adhere to the oral mucosa and deliver an active pharmaceutical agent either directly into the oral mucosa, or into the saliva. Ointments and other sticky adhering compositions have also been used. The active
15 ingredient in all these forms can act locally or systemically. Since the primary goal of these systems is to provide a drug active as opposed to providing a physical barrier to pain, none of the art systems suggest the instant invention.

U.S. Patent No. 4,059,686 describes a sustained-release pharmaceutical preparation for oral cavity adherence and administration to mucosal membranes
20 characterized by being a mixture of a pharmacologically active agent, a pharmaceutical carrier, and sodium polyacrylate in conventional dosage form.

U.S. Patent No. 4,597,959 describes a cosmetic breath freshener composition in wafer form which is said to have slow release properties. The composition includes a multiplicity of microencapsulated liquid droplets of flavoring material
25 contained in an adhesive base.

U.S. Patent No. 4,772,470 discloses an oral bandage comprising a soft adhesive film comprising a mixture of polycarboxylic acid and/or a polycarboxylic acid anhydride and a vinyl acetate polymeric acid anhydride and a vinyl acetate polymer in a compatible state; and an oral preparation comprising such an oral
30 bandage having incorporated therein a topical drug. The oral bandage or preparation is reported to exhibit strong adhesion of long duration when applied to the oral mucosa or teeth.

U.S. Patent No. 4,876,092 describes a sheet-shaped adhesive preparation comprising an adhesive layer containing, as essential components, a carboxyvinyl
35 polymer, a water-insoluble methacrylic copolymer, a polyhydric alcohol, and a pharmaceutically active agent, and a water-impermeable and water-insoluble carrier layer containing, as essential components, a pharmaceutically active, water-

insoluble, film-forming high molecular weight compound and a plasticizer, which can adhere within the mucosal membranes of oral cavity over a period of time and release an active agent.

5 U.S. Patent Nos. 5,160,737 and 5,330,746 disclose a sustained-release liquid polymer or "varnish" composition comprising acrylic polymers (Eudragit® family of polymers) and a pharmaceutical agent. The formulations are useful for preventing dental caries, periodontal disease, and tooth hypersensitivity by brushing or spraying the formulation onto the teeth and gingivae after which liquid polymer dries to a solid film.

10 European Patent Application 223 245 discloses a curable composition containing methacrylate monomers and a polymerization initiator for application to teeth and having the property of in-situ polymerization to form a hardened filler. Use of the filler in combination with an active agent releases the active agent from the hardened filler.

15 Published U.S. application US 2001/0024657 A1, describes a sustained-release solid composition that adheres to hard dentinal surfaces, such as teeth and dentures, and which contains a pharmaceutically active agent. Polyacrylic or polymethacrylic polymers are disclosed as particularly useful in creating an effective controlled-release drug delivery system.

20 Other known preparations usually comprise components which are quickly soluble or disintegrable within the mouth. The pharmaceutically active agents contained in these preparations are mostly swallowed without being absorbed through the mucous membrane in the oral cavity, making these preparations unsatisfactory as sustained- or controlled-release preparations, or as a physical
25 barrier to pain. These known compositions would also be unsatisfactory for permitting substances such as mineralizers, or other systems that interact with saliva and oral flora to create an instant plug or an environment favorable for mineralization, since such actives require time to mature, or time to produce a desired effect, such as tooth whitening or pain relief during eating cold or salty
30 foods.

Accordingly, there is a need for a sustained- or controlled-dissolution oral care composition whose application is easy and uncomplicated, and which can create an immediate barrier to painful stimuli associated with dentinal hypersensitivity, and/or create a barrier to such pain by providing tubule occlusion to the site of pain. The
35 device is disintegrable over time and therefore does not require removal.

SUMMARY OF THE INVENTION

This invention relates to a sustained- or controlled-dissolution composition for the oral cavity that adheres to hard dental surfaces, such as teeth, as well as adjacent soft tissue, thereby forming a barrier to painful stimuli associated with dentinal hypersensitivity. The composition of this invention may also contain an agent effective in reducing the pain associated with dentinal hypersensitivity. Dissolution of the composition is for a predetermined period of time and the agents, if present, at a predetermined concentration. The site of action of the agent is topical and local.

This invention also relates to a sustained- or controlled-dissolution composition capable of reacting with factors in the oral environment to form an insoluble barrier for occluding dentinal tubules. In addition to occluding tubules, the agents useful in creating an insoluble barrier are also useful in reducing dentin wear as a result of acid erosion or mechanical abrasion, such as during tooth brushing.

This invention is also further directed to suitable polymers and/or other barrier-producing compounds and/or cosmetically effective compounds for the oral device. The device can comprise a single self-adherent release layer, or a dual layer comprising a non-adherent layer in combination with a separate adherent layer, or a multilayer structure. If the device comprises a multilayer structure, this enables incompatible compounds to remain separate until contact with heat and/or available water in the oral environment permits their interaction, or the oral environmental factors enable release of nerve desensitizers or barrier-producing compounds, including tubule occluders (e.g., stannous silicate), polymeric tubule occluders (e.g., octadecene/maleic anhydride copolymer, polyacrylic acid/Carbopol, and chitosan), mineralizers (e.g., a soluble calcium source in combination with a soluble phosphate source to produce calcium phosphate, a calcium releasing substrate, such as calcium silicate, hydroxyapatite, arginine carbonate or bioactive glass) or cosmetically relevant compounds.

This invention still further, relates to a method of making and using the sustained- or controlled-dissolution compositions described herein.

DETAILED DESCRIPTION OF THE INVENTION

The term "barrier" as used herein at all occurrences means, a structure that hinders or prevents those factors associated with dentinal hypersensitivity from reaching the nerve, thereby reducing or eliminating the pain associated with dentinal hypersensitivity. Therefore, the term barrier suitably includes a solid polymeric oral care device or film that adheres to the teeth and surrounding soft tissue and/or a

precipitate generated *in situ*, at the site of pain, and which occludes the dentinal tubules.

In the case of a device or film, the composition may be in the form of an extruded or cast film which is applied directly to the desired site, forming a barrier which dissolves over time. In an alternative embodiment, the composition may be in the form of a gel, paste, semi-solid balm, spray, and the like, all of which form a physical barrier *in situ*, which physical barrier dissolves over time.

The sustained- or controlled-dissolution composition of this invention is intended to prevent and/or treat dentinal hypersensitivity. This is achieved by (a) creating a physical barrier to painful stimuli at the site of sensitivity, (b) supplying agents to the site, which agents are capable of creating a physical barrier to painful stimuli, and/or (c) interacting with the oral environment, for example, saliva, to form a precipitate for occluding dentinal tubules.

The composition of this invention is capable of adhering to natural teeth or surrounding soft tissue and comprises at least one water-swellaable or water-soluble polymer. Suitable polymers include, but are not limited to, cellulose derivatives, such as ethyl cellulose (for example, Ethocel St-10, manufactured by Dow Chemical Company, located in Midland, Michigan), hydroxypropylmethyl cellulose ("HPMC"), hydroxypropyl cellulose ("HPC"), carboxymethyl cellulose ("CMC"), polyethylene oxide ("Polyox®"), chitosan, starch, alginic acid and salts thereof, alkali metal salts of alkylvinylether/maleic acid or anhydride copolymer ("Gantrez®"), and mixtures thereof.

Suitably, the oral care composition may be in the form of an extruded film or cast/evaporated film. In addition, the oral care composition may be in the form of a gel, paste, spray, semi-solid balm, and the like, all of which form a physical barrier upon application to the site of pain.

The oral care composition described herein is capable of dissolving over time. The time frame within which the composition dissolves depends upon the desired use. So, for example, the composition can be formulated for "spot relief", that is where the dissolution time is from about 1 to 5 minutes. Or, the composition can be formulated for more sustained dissolution, for example to correspond to an event such as a meal, that is where the dissolution time is from about 30 to 60 minutes. Further, the composition can be formulated for long term dissolution, for example to provide pain relief for an entire day. In order to achieve varying dissolution times, the skilled artisan would manipulate the polymers used in the composition. For example, HPC dissolves much slower than HPMC. By varying the concentration of one or more of these polymers in the composition, one of skill

in the art could formulate a product that dissolves at varying rates of time. The sustained- or controlled-dissolution of this composition is essential to its performance as a barrier to painful stimuli, and/or, as a composition capable of providing a tubule-occluding barrier to painful stimuli directly to the site of pain.

5 For treating hypersensitivity, the composition of the invention may be used as a barrier to the painful stimuli associated with dentinal hypersensitivity. For example, a person sensitive to food items will apply the oral care composition claimed herein to the area of sensitivity just prior to ingesting such food, for example, ice cream. The instant composition would serve as a barrier to the cold, as
10 well as air stimuli, and slowly dissolve over time, or at least in time for the meal to be completed.

In addition to providing a physical barrier to painful stimuli associated with dentinal hypersensitivity, the instant composition can also contain a nerve desensitizer which acts at the site of pain while concurrently providing a physical
15 barrier to pain. In this way, the composition provides the immediate pain relief benefit of a physical barrier, while also providing the prolonged benefit of a nerve desensitizer, acting at the site of pain even after the composition has dissolved.

Suitable nerve desensitizing agents include, but are not limited to, potassium salts, for example, potassium nitrate, potassium chloride, potassium bicarbonate, and
20 potassium citrate, strontium salts, for example, strontium chloride, strontium acetate, strontium nitrate, and strontium fluoride, and a combination of zinc and strontium ions, or mixtures thereof.

The nerve-desensitizing agent is incorporated in the composition in a desensitizing effective amount. This will vary depending on the particular shape and
25 thickness of the solid oral care composition used. Suitably, the nerve agent will be present in an amount of about 0.1 to 15 wt.%, preferably from about 0.3 to 10 wt.%, and most preferably from about 2 to 8 wt.%.

In addition to serving as a physical barrier to painful stimuli associated with dentinal hypersensitivity, the instant composition can also create a physical barrier
30 by being comprised of agents which are capable of occluding the dentinal tubules.

Agents capable of occluding the dentinal tubules can do so by reacting with the oral environment to create a precipitate which occludes the tubules through a process called mineralization. Suitably, agents which occlude dentinal tubules by mineralization are included in the scope of this invention and include, but are not
35 limited to, a soluble calcium source in combination with a soluble phosphate source to produce calcium phosphate, a calcium releasing substrate, such as calcium silicate, hydroxyapatite, arginine carbonate or bioactive glass. Mineralization can

occur when the oral care composition is exposed to saliva containing calcium and/or phosphate.

Agents capable of occluding dentinal tubules can also do so without mineralization. One way is by forming a non-mineral precipitate, for example, by "salting-out" a compound precipitate capable of occluding the tubules. This can be done by manipulating the pH of the composition when it encounters the oral environment, or when the composition is exposed to ions in the saliva. Suitably, agents which occlude dentinal tubules without mineralization are also included within the scope of this invention and include, but are not limited to, inorganic tubule occluders, for example, stannous silicate, and polymer tubule occluders, for example, sodium alginate, octadecene/maleic anhydride copolymer, polyacrylic acid/Carbopol, and chitosan.

Suitable occluders can be found in WO 02/15809, incorporated herein by reference. The tubule blocking agent/occluder is incorporated in this composition in a desensitizing tubule occluding effective amount. The amount will vary depending on the particular shape and thickness of the solid oral care composition used. Suitably, the tubule blocking agent will be in an amount of about 0.1 to 15 wt.%, preferably from about 0.4 to 10% and most preferably from about 2 to 8 wt.%. Phosphate, coco and alike soaps such as MAPS (Rhodia), may be incorporated to further enhance the physical occlusion. Larger amounts of the tubule blocking agent can also be employed if desired.

The composition of this invention is also suitable for use in preventing the hypersensitivity associated with tooth whitening preparations. Further uses of the instant compositions include, but are not limited to, treating gingivitis and preventing caries. By creating a physical barrier, the instant composition prevents exposure of the sensitive areas to irritants, food acid, bacteria and other factors in the oral environment which cause sensitivity, disease or pain.

The sustained- or controlled-dissolution compositions containing the desensitizing attributes of the present invention may contain additional ingredients typically incorporated into oral care compositions. Suitable ingredients include, without limitation, a fluoride source, flavoring agents, humectants, binders and sweetening agents.

Humectants contemplated for use in these compositions include, but are not limited to, polyols, such as glycerol, sorbitol, polyethylene glycols, propylene glycol, hydrogenated partially hydrolyzed polysaccharides, and the like. The humectants are generally present in amounts of from 0 to 80 wt.%. Thickeners

suitable for use in the invention, for example silica, may be present at a level from about 0 to 50 wt.%.

Binders suitable for use in the compositions of the invention include, but are not limited to, hydroxyethyl cellulose, and hydroxypropyl cellulose, as well as xanthan gums, Iris moss and gum tragacanth. Binders may be present in the amount from 0.01 to 100 wt.%. Sweeteners suitable for use, e.g., saccharin, may be present at levels of about 0 to 5 wt.%.

Fluoride sources commonly used in oral health care compositions, such as sodium fluoride, stannous fluoride, sodium monofluorophosphate, zinc ammonium fluoride, tin ammonium fluoride, calcium fluoride, amine fluoride, and cobalt ammonium fluoride may be included for delivering anti-caries benefit. If present, fluoride ions are typically provided at a level of from 0 to 1500 ppm, preferably 50 to 1500 ppm, although higher levels up to about 3000 ppm may be used.

Suitable flavors are usually included in low amounts, such as from 0 to about 5 wt.%. Dyes/colorants suitable for oral health care compositions, i.e., FD & C Blue #1, FD & C Yellow #10, FD & C Red #40, etc., may be employed as well.

Suitably, the instant composition may also include other pharmaceutically or cosmetically active agents requiring local application, for example, local anesthetics, for example, eugenol, dibucaine hydrochloride, dibucaine, lidocaine hydrochloride, lidocaine, bezocaine, p-buthylaminobenzoic acid 2-(di-ethylamine ethyl ester hydrochloride, procaine hydrochloride, tetracaine hydrochloride, chloroprocaine hydrochloride, oxyprocaine, hydrochloride, mepivacaine, cocaine hydrochloride, and piperocaine hydrochloride, tooth whitening agents, for example, sodium tripolyphosphate, urea peroxide, hydrogen peroxide, and peroxide releasing agents, such as perborate or percarbonate. Also included may be pH adjusting agents; anti-caries agents such as calcium glycerophosphate, sodium trimetaphosphate; anti-staining compounds such as silicone polymers, plant extracts and mixtures thereof.

The oral care device of this invention can comprise any shape or thickness suitable for application to a discreet area in the mouth. The oral care device may be a square, rectangle, circle, semi-circle, or other geometry, consideration being given to the area to be covered, and the desire to reduce the "foreign feeling" of having the device in the mouth. Suitably, the oral care device is 0.1-50 mm thick, preferably 3-5mm, depending upon the structure (e.g., single or multi-layered), the desired dissolution time, and the presence of active ingredients.

Suitably, the oral care device can be multi-layered with incompatible materials in separate layers (such as zinc and/or calcium and phosphate and/or

silicate), and/or one adhesive layer, the other non-adhesive (so as to stick to gingiva and teeth but not the cheek or tongue).

In an alternative embodiment, the composition can be administered in the form of a spray, paste, gel, semi-solid balm, and the like. If delivered in one of these forms, the composition will form a film upon contact with the tooth surface creating a physical barrier to painful stimuli, and thereafter dissolve over time.

The invention will now be illustrated in greater detail with reference to the following examples, but it should be understood that these are not intended to limit the present invention.

10

EXAMPLES:

Example 1: illustrates the use of a cationic polymer for making a composition of the invention, which polymer is compatible with other cationic ingredients for inclusion in the composition, for example, stannous ions, zinc ions and cetylpyrrolidinium chloride ("CPC").

15

	<u>INGREDIENT</u>	<u>%w/w</u>
	Chitosan	2.0
	Glycerin	0.5
20	SnF ₂	90ppm
	Zn lactate	1.0
	Lactic acid	2.0
	Sn gluconate	0.5
	CPC	0.2
25	Water	Q.S.

Example 2: illustrates the use of non-ionic polymer for making a composition of the invention.

30	<u>INGREDIENT</u>	<u>%w/w</u>
	HEC	0.25
	Water	Q.S.
	HPC	4.50
	HPMC	0.25
35	Triclosan	0.02

Example 3: illustrates the use of anionic polymers for making a composition of the invention, which polymer is compatible with other anionic ingredients for inclusion in the composition, for example, alginic acid, Polyox®, and CMC.

5	<u>INGREDIENT</u>	<u>%w/w</u>
	Alginic acid	1.0
	HPC	3.0
	Polyox®	0.5
	CMC	0.3
10	Na/Ca Gantrez	0.3
	Silicon Dioxide	0.1
	PEG 600	0.5
	SrCl ₂	0.6
	Water	Q.S.

15

Example 4: illustrates a formulation of the invention useful for preventing the pain associated with tooth whitening.

	<u>INGREDIENT</u>	<u>%w/w</u>
20	HEC	0.25
	Water	Q.S.
	Silaceous mineralizer	1.00
	HPC	4.50
	HPMC	0.25
25	Urea peroxide	0.80

The above films are made by dissolving the ingredients in water with suitable agitation, and pouring the mixture onto a casting plate. The liquid is dried by air at room temperature, or in a vacuum oven at elevated temperatures. For those compositions with reactive agents, such as urea peroxide, the reactive agents can be added after some drying of the composition occurs, in order to prevent reaction in solution. The film can then be cut in any geometry desired.

30

Examples 5 through 7 illustrate extruded films that are made according to this invention. Conventional techniques known in the art for making extruded films can be applied to the instant invention.

Example 5:

	<u>INGREDIENT</u>	<u>%w/w</u>
	Polylysine	10.0
5	HPC	Q.S.
	Chitosan	5.0
	Citric acid	5.0
	Glycerin	3.0
	Chlorhexidine	0.1
10		

Example 6:

	<u>INGREDIENT</u>	<u>%w/w</u>
	HPC	80
	SiO ₂	2.5
15	HEC	4.0
	HPMC	1.5
	PEG 1450	4.0
	Urea peroxide	8.0
	Flavor	0.1
20		

Example 7:

	<u>INGREDIENT</u>	<u>%w/w</u>
	Polyox	45.0
	CMC	3.0
25	HPC	5.0
	Na/Ca Gantrez	15.0
	Silicon Dioxide	3.0
	PEG 600	0.1
	Starch	5.0
30	KNO ₃	3.8
	Water	25.0

Example 8: illustrates a two-layer system according to the invention.

Layer 1:

	<u>INGREDIENT</u>	<u>%w/w</u>
	SnF ₂	500ppm
5	SnCl ₂	1.0
	HPC	90.0
	Water	Q.S.

Layer 2 (tooth side):

	<u>INGREDIENT</u>	<u>%w/w</u>
10	Potassium silicate	1.0
	SiO ₂	2.5
	HPC	90.0
	Water	Q.S.

15

Example 9: Illustrates a film forming paste. In this Example Carbopol was dispersed in the ethanol. Glycerol was added and mixture stirred until material thickens. Ethocel was added. A second mixture was prepared containing the molten petrolatum, PEG 400, clove oil and the silica dispersed in the mixture. To the petrolatum silica dispersion was added the ethocel mixture with stirring. And blend thoroughly until mixture was homogeneous. Cooled gel was packed into tubes. This material sticks readily to wet surfaces.

	<u>INGREDIENT</u>	<u>%w/w</u>
25	Petrolatum	22.0
	Sident 22	5.00
	Carbopol 974P	3.00
	Clove oil	1.00
	Ethocel St-10	10.0
30	Ethanol	30.0
	Glycerol	20.0
	PEG 400	10.0

Example 10: Illustrates a film forming gel. Ethyl cellulose was dispersed in the ethanol. A second mixture containing the molten petrolatum, mineral oil, clove oil and the silica dispersed therein, was prepared. To the petrolatum silica dispersion was added the ethocel mixture with stirring. The mixture was blended
5 thoroughly until it was homogeneous. This mixture can be packed in tubes or pen applicators and spread on teeth with a finger or brush.

	<u>INGREDIENT</u>	<u>%w/w</u>
	Petrolatum	10.0
10	Sident 22	10.0
	Mineral oil	20.0
	Clove oil	1.00
	Ethocel St-10	10.0
	Gantrez M955	14.0
15	Ethanol	35.0

Example 11: Illustrates a film forming spray. Ethyl cellulose was dispersed in the ethanol and triethyl citrate. A second mixture was prepared containing the molten petrolatum, mineral oil and clove oil and the silica dispersed in it. To the
20 petrolatum mixture was added the ethyl cellulose mixture with stirring. This mixture was blended thoroughly until mixture was homogeneous. The mixture can be sprayed onto wet surfaces from a pump spray.

	<u>INGREDIENT</u>	<u>%w/w</u>
25	Petrolatum	20.0
	Mineral oil	15.0
	Clove oil	1.00
	Ethocel St-10	10.0
	Triethyl citrate	2.00
30	Ethanol	53.0

All publications, including, but not limited to, patents and patent applications cited in this specification, are herein incorporated by reference as if each individual publication were specifically and individually indicated to be incorporated by reference
35 herein as though fully set forth.

The above description fully discloses the invention including preferred embodiments thereof. Modifications and improvements of the embodiments specifically disclosed herein are within the scope of the following claims. Without further elaboration it is believed that one skilled in the art can, given the preceding description, 5 utilize the present invention to its fullest extent. Therefore any examples are to be construed as merely illustrative and not a limitation on the scope of the present invention in any way. The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows.

What is claimed is:

1. A controlled-dissolution oral care composition for adherence to natural teeth and adjacent soft tissue comprising at least one water-swellable or
5 water-soluble polymer, which composition creates a physical barrier to painful stimuli associated with dentinal hypersensitivity.
2. The controlled-dissolution oral care composition according to claim 1, wherein the polymer is selected from, cellulose derivatives, polyethylene oxide,
10 chitosan, starch, alginic acid and salts thereof, alkali metal salts of alkylvinylether/maleic acid or anhydride copolymer, and mixtures thereof.
3. A controlled-dissolution oral care composition for adherence to natural teeth and adjacent soft tissue comprising at least one water-swellable or
15 water-soluble polymer and a nerve desensitizing agent, which composition creates a physical barrier to painful stimuli associated with dentinal hypersensitivity.
4. The controlled-dissolution oral care composition of claim 3, wherein the nerve desensitizing agent is selected from a potassium salt, a strontium salt, or a
20 combination of zinc or strontium ions, and mixtures thereof.
5. A controlled-dissolution oral care composition for adherence to natural teeth and adjacent soft tissue comprising at least one water-swellable or water-soluble polymer and a mineralizing agent, which composition creates a
25 physical barrier to painful stimuli associated with dentinal hypersensitivity.
6. The controlled-dissolution oral care composition of claim 5, wherein the mineralizing agent is selected from a soluble calcium source in combination with a soluble phosphate source to produce calcium phosphate, a calcium releasing
30 substrate, hydroxyapatite, arginine carbonate or bioactive glass.
7. A controlled-dissolution oral care composition for adherence to natural teeth and adjacent soft tissue comprising at least one water-swellable or

water-soluble polymer and an agent capable of forming a non-mineral precipitate for occluding dentinal tubules, which composition creates a physical barrier to painful stimuli associated with dentinal hypersensitivity.

5 8. The controlled-dissolution oral care composition according to claim 7, wherein the agent capable of forming a non-mineral precipitate is selected from an inorganic tubule occluder or a polymer tubule occluder.

 9. The controlled-dissolution oral care composition according to claim
10 8, wherein the polymer tubule occluder is selected from sodium alginate, octadecene/maleic anhydride copolymer, polyacrylic acid or chitosan.

 10. A composition as claimed in any of the preceeding claims wherein
15 the composition is in the form of a patch, a spray, a gel, a stick or a paste.

 11. A method of treating and/or preventing tooth hypersensitivity by
applying a composition according to any of the preceeding claims to the tooth
surface.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/36491

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61C 5/00 US CL : 433/217.1 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 433/217.1, 215, 228.1; 424/49, 52, 57 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,334,375A (NABI et al.) 02 August 1994 (02.08.1994), see entire document.	1,2,5,6,10,11
X	US 5,849,266A (FRIEDMAN) 15 December 1998 (15.12.1998), see entire document.	1-4,7-11
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 29 March 2004 (29.03.2004)		Date of mailing of the international search report 22 APR 2004
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230		Authorized officer Melba Sumgataci Telephone No. 703-308-0858

PATENT COOPERATION TREATY

PCT

REC'D 13 JUL 2005

INTERNATIONAL PRELIMINARY EXAMINATION REPORT **WIPO** **PCT**

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference C75129		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US03/36491	International filing date (day/month/year) 14 November 2003 (14.11.2003)	Priority date (day/month/year) 14 November 2002 (14.11.2002)	
International Patent Classification (IPC) or national classification and IPC IPC(7): A61C 5/00 and US Cl.: 433/217.1			
Applicant SMITHKLINE BEECHAM CORPORATION			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of ___ sheets.</p> <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand 27 May 2004 (27.05.2004)		Date of completion of this report 24 June 2005 (24.06.2005)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer Melba Bumgarner <i>Diane Smith</i> Telephone No. 703-308-0858	

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/36491

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-15 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the claims:
pages 16 and 17 as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/36491**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-11</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-11</u>	NO
Industrial Applicability (IA)	Claims <u>1-11</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-11 lack novelty under PCT Article 33(2) as being anticipated by Nabi et al. Nabi et al. disclose an oral care composition comprising methyl vinyl ether/maleic anhydride copolymer and a potassium salt, an oral care composition comprising methyl vinyl ether/maleic anhydride copolymer and anhydrous dicalcium phosphate, and an oral care composition comprising methyl vinyl ether/maleic anhydride copolymer and polyacrylic acid, all in the form of a paste or gel. Nabi et al. show a method of applying the composition to the tooth surface.

Claims 1-4, 10, and 11 lack novelty under PCT Article 33(2) as being anticipated by Friedman. Friedman discloses an oral care composition comprising cellulose derivatives and strontium chloride in the form of a spray. Friedman shows a method of treating tooth hypersensitivity by applying the composition to the tooth surface.

Claims 1-11 meet the criteria set out in PCT Article 33(4), and thus meet industrial applicability because the subject matter claimed can be made or used in industry.

----- NEW CITATIONS -----